	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	350	(dipeptidyl adj peptidase adj IV) or (DP adj IV)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:35			0
2	BRS	L2	211	1 same inhibit$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:36			0
3	BRS	L3	7	2 same (unstable or masked)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:37			0
4	BRS	L4	3	(Ile-thia) or (ile-pyr) or (val-thia) or (val-pyr)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:48			0
5	BRS	L5	1	(dipeptidyl adj alkyl adj ketone) or (dipeptidyl adj fluoroalkyl adj ketone) or (dipeptidyl adj chloroalkyl adj ketone) or (dipeptidyl adj cyanide) or (dipeptidyl adj pyridium adj methyl adj ketone)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:50			0
6	BRS	L6	815660	acetate or succinate or tartrate or fumarate or phosphate or sulfate	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:52			0
7	BRS	L7	0	3 same 6	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:52			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
8	BRS	L8	45472	(metabolic adj disorder) or diabetes or (impaired adj glucose adj toterance) or (diabetic adj neuropathy) or nephrapathy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:55			0
9	BRS	L9	2	3 same 8	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/16 19:55			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L7	7	(((dipeptidyl adj peptidase adj IV) or (DP adj IV)) same inhibit$3) same (unstable or masked)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:36			0
2	BRS	L8	3040	(alkyl adj ketone) or (fluoroalkyl adj ketone) or (chloroalkyl adj ketone) or (peptide adj cyanide) or (pyridium adj methyl adj ketone)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:37			0
3	BRS	L9	211	((dipeptidyl adj peptidase adj IV) or (DP adj IV)) same inhibit$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:38			0
4	BRS	L10	2	8 same 9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:45			0
5	BRS	L11	27	demuth adj hans-ulrich.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:46			0
6	BRS	L12	0	schimdt adj jorn.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:46			0
7	BRS	L13	40	hoffmann adj torsten.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:47			0
8	BRS	L14	13	glund adj konrad.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:47			0
9	BRS	L15	3	(7 or 10) and (11 or 13 or 14)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/01/17 09:48			0

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FILE 'HOME' ENTERED AT 19:59:44 ON [redacted] JAN 2003

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 20:00:10 ON 16 JAN 2003

FILE 'CAPLUS' ENTERED AT 20:00:10 ON 16 JAN 2003
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FILE 'SCISEARCH' ENTERED AT 20:00:10 ON 16 JAN 2003
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FILE 'AGRICOLA' ENTERED AT 20:00:10 ON 16 JAN 2003

=> s (dipeptidyl peptidase IV) or (dp IV)
L1        5816 (DIPEPTIDYL PEPTIDASE IV) OR (DP IV)

=> s l1 (p) inhibit?
L2        1726 L1 (P) INHIBIT?

=> s l2 (p) (unstable or masked)
L3          14 L2 (P) (UNSTABLE OR MASKED)

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L3
L4            5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)

=> d l4 1-5 ibib abs

L4   ANSWER 1 OF 5     MEDLINE                          DUPLICATE 1
ACCESSION NUMBER:   2001410442     MEDLINE
DOCUMENT NUMBER:    21235368   PubMed ID: 11337057
TITLE:              Transbuccal peptide delivery: stability and in vitro
                    permeation studies on endomorphin-1.
AUTHOR:             Bird A P; Faltinek J R; Shojaei A H
CORPORATE SOURCE:   Department of Pharmaceutical Sciences, School of Pharmacy,
                    Texas Tech University Health Sciences Center, Amarillo, TX
                    79106, USA.
SOURCE:             JOURNAL OF CONTROLLED RELEASE, (2001 May 18) 73 (1) 31-6.
                    Journal code: 8607908. ISSN: 0168-3659.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200107
ENTRY DATE:         Entered STN: 20010723
                    Last Updated on STN: 20010723
                    Entered Medline: 20010719
AB   The purpose of this study was to investigate the feasibility of buccal
     delivery of a model peptide, endomorphin-1 (ENI), using stability and in
     vitro permeation studies. ENI is a recently isolated mu-opiate receptor
     agonist with high selectivity and specificity for this receptor subtype.
     Stability studies were conducted in various buffers and the drug was shown
     to be stable in both acidic and basic buffer systems. In the presence of
     full thickness porcine buccal epithelium, ENI was   ***unstable***   with
     only 23.4+/-15.7% intact drug present after 6 h. The region responsible
     for this degradation was found to coincide with the major barrier region
     of the buccal epithelium as delineated through stability experiments in
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the presence of partial thickness buccal epithelium. Various peptidase ***inhibitors*** were used to isolate the enzyme(s) responsible for this degradation. Diprotin-A, a potent ***inhibitor*** of ***dipeptidyl*** ***peptidase*** ***IV*** , provided significant ***inhibition*** of the degradation of ENI in the presence of buccal epithelium. In vitro permeation studies revealed that the permeability coefficient of ENI across porcine buccal epithelium was 5.67+/-4.74x10(-7) cm/s. The enzymatic degradation of ENI was found not to be rate limiting to the drug's permeation across buccal epithelium, as diprotin-A did not increase the permeation of ENI. Sodium glycocholate as well as sodium taurocholate were also ineffective in enhancing the permeation of ENI across porcine buccal epithelium.

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:819402 CAPLUS
DOCUMENT NUMBER: 132:36038
TITLE: Synthesis of prodrugs of ***unstable*** ***dipeptidyl*** ***peptidase*** ***IV*** ***inhibitors*** for use in treating diabetes
INVENTOR(S): Demuth, Hans-Ulrich; Schmidt, Jorn; Hoffmann, Torsten; Glund, Konrad
PATENT ASSIGNEE(S): Probiodrug Gesellschaft Fur Arzneimittelforschung m.b.H., Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967279	A1	19991229	WO 1999-EP4381	19990624
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19828114	A1	20000127	DE 1998-19828114	19980624
CA 2335978	AA	19991229	CA 1999-2335978	19990624
AU 9947772	A1	20000110	AU 1999-47772	19990624
BR 9911415	A	20010320	BR 1999-11415	19990624
EP 1090030	A1	20010411	EP 1999-931163	19990624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002518518	T2	20020625	JP 2000-555930	19990624
NO 2000006483	A	20001219	NO 2000-6483	20001219
US 2001020006	A1	20010906	US 2000-745883	20001221

PRIORITY APPLN. INFO.: DE 1998-19828114 A 19980624
WO 1999-EP4381 W 19990624

OTHER SOURCE(S): MARPAT 132:36038
GI

/ Structure 1 in file .gra /

AB The invention relates to compds. of ***unstable*** ***inhibitors*** of ***dipeptidyl*** ***peptidase*** ***IV*** (***DP*** ***IV***) which comprise general formula A-B-C, whereby A represents an amino acid, B represents the chem. bond between A and C or an amino acid, and C represents an ***unstable*** ***inhibitor*** of ***DP*** ***IV*** . Such compds. are used for treating altered glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic neuropathy, nephropathy, and secondary diseases in mammals caused by diabetes mellitus. Thus, (I) was reacted with pyridine to give [(II); R = Cbz], which was deprotected to give II (R = H)(III) which is thought to undergo an intramol. cyclization (no data) to form the active

DP ***IV*** ***inhibitor*** . In 0.1 M HEPES-buffer, pH 7.6, at 25.degree., III had a [redacted]lf life (before self-cyclizati[redacted] of 13.3 min.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1998327123 MEDLINE
DOCUMENT NUMBER: 98327123 PubMed ID: 9660870
TITLE: Functional specialization of stable and dynamic microtubules in protein traffic in WIF-B cells.
AUTHOR: Pous C; Chabin K; Drechou A; Barbot L; Phung-Koskas T; Settegrana C; Bourguet-Kondracki M L; Maurice M; Cassio D; Guyot M; Durand G
CORPORATE SOURCE: Laboratoire de Biochimie Generale, Equipe d'Accueil 1595, Unite de Formation et de Recherche de Pharmacie, Universite Paris-Sud, 92296 Chatenay-Malabry, France.
SOURCE: JOURNAL OF CELL BIOLOGY, (1998 Jul 13) 142 (1) 153-65. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980820
AB We found that the magnesium salt of ilimaquinone, named 201-F, specifically disassembled dynamically ***unstable*** microtubules in fibroblasts and various epithelial cell lines. Unlike classical tubulin-interacting drugs such as nocodazole or colchicine which affect all classes of microtubules, 201-F did not depolymerize stable microtubules. In WIF-B-polarized hepatic cells, 201-F disrupted the Golgi complex and ***inhibited*** albumin and alpha1-antitrypsin secretion to the same extent as nocodazole. By contrast, 201-F did not impair the transport of membrane proteins to the basolateral surface, which was only affected by the total disassembly of cellular microtubules. Transcytosis of two apical membrane proteins-the alkaline phosphodiesterase B10 and ***dipeptidyl*** ***peptidase*** ***IV*** -was affected to the same extent by 201-F and nocodazole. Taken together, these results indicate that only dynamically ***unstable*** microtubules are involved in the transport of secretory proteins to the plasma membrane, and in the transcytosis of membrane proteins to the apical surface. By contrast, stable microtubules, which are not functionally affected by 201-F treatment, are involved in the transport of membrane proteins to the basolateral surface. By specifically disassembling highly dynamic microtubules, 201-F is an invaluable tool with which to study the functional specialization of stable and dynamic microtubules in living cells.

L4 ANSWER 4 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95220827 EMBASE
DOCUMENT NUMBER: 1995220827
TITLE: Amino acid and peptide phosphonate derivatives as specific inhibitors of serine peptidases.
AUTHOR: Oleksyszyn J.; Powers J.C.
CORPORATE SOURCE: OsteoArthritis Sciences, Inc.,Cambridge, MA 02139, United States
SOURCE: Methods in Enzymology, (1994) 244/- (423-441). ISSN: 0076-6879 CODEN: MENZAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters have a number of advantages for in vitro and in vivo experiments compared to other commonly used peptide serine peptidase ***inhibitors*** . They are easily synthesized, are chemically very stable, and are not alkylating agents such as the commonly used peptide chloromethyl ketone serine peptidase ***inhibitors*** . They are more stable than most other organophosphorus ***inhibitors*** , including peptidyl derivatives of

the .alpha.-aminoalkyl phosphonates, where the phosphonate moiety is chemically activated by the presence of better leaving groups. The .alpha.-aminoalkyl phosphonate diphenyl esters have outstanding stability (t(1/2) usually greater than 4 days at pH 7.5; >24 hr in plasma). Thus, low ***inhibitor*** concentrations can effectively control unwanted serine peptidase activity with low ***inhibitor*** concentrations over long time periods, which makes them perfect tools for experiments involving cells. Because .alpha.-aminoalkyl phosphonate diphenyl esters are irreversible ***inhibitors*** , they offer real advantages in many experimental situations over reversible ***inhibitors*** in cases in which it may be necessary to maintain high concentrations of the reversible ***inhibitor*** for long time periods. The second-order ***inhibition*** rate constants for phosphonate ***inhibitors*** are usually not as high as those observed with other types of peptidyl serine peptidase ***inhibitors*** . This is compensated for by their high stability and specificity. The irreversible character of the ***inhibition*** reaction allows effective ***inhibition*** even if the inactivation rate constant is not large. For example, Cbz-Val(P)(OPh)2 ***inhibits*** HLE with a rate constant of 260 M-1 sec-1. Thus at an effective concentration of 10 .mu.M, 50% of the enzyme is inactivated after 4.5 min, and almost no activity is detected after an 11-min incubation time. Frequently there is a need to specifically ***inhibit*** serine peptidases in vitro during protein purification procedures or in biological experiments involving cells or tissue culture. Typically, peptide chloromethyl ketone derivatives are used. However, these inactivators are quite nonspecific alkylating agents and experimental results can be misleading. For example, the presence of a chymotrypsin-like enzyme activity on the neutrophil membrane was assumed when ***inhibition*** with Tos-Phe-CH2Cl resulted in ***inhibition*** of the so-called oxidative burst of these cells. However, it has been shown that the targeted protein is not a serine peptidase, and ***inhibition*** results from a nonspecific alkylation reaction. As another example of the utility of phosphonates, dipeptide derivatives of .alpha.-aminoalkyl phosphonate diphenyl ester derivatives with a P1 proline residue are effective ***inhibitors*** for ***dipeptidyl*** - ***peptidase*** ***IV*** . The corresponding dipeptide boronic acid and chloromethyl ketone derivatives are ***unstable*** . In summary, peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters are highly specific irreversible ***inhibitors*** of serine peptidases and are chemically stable and stable in plasma. They offer a number of advantages over other types of ***inhibitors*** currently in use in biological experiments. After reaction with the enzyme, they form very stable enzyme- ***inhibitor*** complexes, making them interesting tools for X-ray studies on the active site structure of new serine peptidases.

L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 1982:522831 CAPLUS
DOCUMENT NUMBER: 97:122831
TITLE: Dipeptidyl peptidase IV inhibits the polymerization of fibrin monomers
AUTHOR(S): Mentlein, Rolf; Heymann, Eberhard
CORPORATE SOURCE: Med. Fak., Univ. Kiel, Kiel, D-2300, Fed. Rep. Ger.
SOURCE: Archives of Biochemistry and Biophysics (1982), 217(2), 748-50
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A highly purified ***dipeptidyl*** ***peptidase*** ***IV*** (I) from human placenta cleaved glycylproline from the N-terminal end of the fibrin .alpha. chain and ***inhibited*** the clotting of fibrin monomers. This result underlined the importance of the N-terminus of the fibrin .alpha. chain as an aggregation site ***masked*** by fibrinopeptide A. Apparently, I can hinder blood coagulation in intact vessels in vivo, because it is located on the surface of the capillary endothelium.

=> s (dipeptidyl alkyl ketone) or (dipeptidyl fluoroalkyl ketone) ot (dipeptidyl chloroalkyl keton
MISSING OPERATOR KETONE) OT
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

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=> s (dipeptidyl alkyl ketone)
L5            0 (DIPEPTIDYL ALKYL KETONE)

=> s (dipeptidyl fluoroalkyl ketone)or  (dipeptidyl chloroalkyl ketone) or (dipeptidyl cyanide) or
L6            1 (DIPEPTIDYL FLUOROALKYL KETONE) OR (DIPEPTIDYL CHLOROALKYL KETON
                E) OR (DIPEPTIDYL CYANIDE) OR (DIPEPTIDYL PYRIDIUM METHYL KETONE
                )

=> d l6 1 ibib abs

L6   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:142666  CAPLUS
DOCUMENT NUMBER:          136:200479
TITLE:                    Preparation of proline derivatives as dipeptidyl
                          peptidase IV (DPP-IV) inhibitors and use thereof as
                          drugs
INVENTOR(S):              Kitajima, Hiroshi; Sakashita, Hiroshi; Akahoshi,
                          Fumihiko; Hayashi, Yoshiharu
PATENT ASSIGNEE(S):       Welfide Corporation, Japan
SOURCE:                   PCT Int. Appl., 340 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ----------------  ----  --------       ---------------  --------
     WO 2002014271      A1   20020221       WO 2001-JP6906   20010810
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2001077754      A5   20020225       AU 2001-77754    20010810
PRIORITY APPLN. INFO.:                   JP 2000-243217   A  20000810
                                         JP 2000-400296   A  20001228
                                         WO 2001-JP6906   W  20010810
OTHER SOURCE(S):          MARPAT 136:200479
GI
```



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/ Structure 2 in file .gra /
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AB The title compds. [I; X = NR1R2, NR3COR4, NR5COR4, NR5CH2CH2NR6R7, NR8SO2R9, OR10, O2CR11; wherein R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, or they are linked to each other to form a heterocyclyl contg. 1 or 2 N atoms or O which may be a spiro ring and is optionally fused to an (un)substituted arom. ring; R3, R4 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, arylalkenyl, heteroaryl, heteroarylalkyl; R5, R6, R7 = H, alkyl, acyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl, or which is optionally fused to an (un)substituted arom. ring; R8, R9, R10, R11 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl] or pharmacol. acceptable salts thereof are prepd. These compds. are useful for the treatment of DPP-IV related diseases such as diabetes, obesity, HIV infection, cancer metastasis, skin diseases, prostatic hypertrophy (prostatomegaly), pericementitis, or autoimmune diseases. Thus, a soln. of 0.924 g (S)-1-[(2S,4S)-4-amino-1-tert-butoxycarbonyl-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine (prepn. given), 1.7 mL diisopropylethylamine, and 0.78 g 2-chloro-4-fluorobenzonitrile in 10 mL N-methyl-2-pyrrolidone were stirred at 80.degree. for 4 h to give 0.94 g (S)-1-[(2S,4S)-1-tert-butoxycarbonyl-4-(3-chloro-4-cyanophenyl)amino-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine

which (0.93 g) was treated with HCl/EtOAc at room temp. for 15 h to give (S)-1-[(2S,4S)-4-(3-chloro-4-[redacted]nophenyl)amino-2-pyrrolidinyl[redacted]onyl]-2-cyanopyrrolidine hydrochloride (II). II showed IC50 of 0.13 and 0.15 nM against human blood plasma DPP-IV and rat blood plasma DPP-IV, resp.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 19:59:44 ON 16 JAN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 20:00:10 ON 16 JAN 2003
L1 5816 S (DIPEPTIDYL PEPTIDASE IV) OR (DP IV)
L2 1726 S L1 (P) INHIBIT?
L3 14 S L2 (P) (UNSTABLE OR MASKED)
L4 5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)
L5 0 S (DIPEPTIDYL ALKYL KETONE)
L6 1 S (DIPEPTIDYL FLUOROALKYL KETONE)OR (DIPEPTIDYL CHLOROALKYL KE

=> s acetate or succinate or tartrate or fumarate or phosphate or sulfate
5 FILES SEARCHED...
L7 2933765 ACETATE OR SUCCINATE OR TARTRATE OR FUMARATE OR PHOSPHATE OR SULFATE

=> s l7 (p0 l4
MISSING OPERATOR 'L43 (P0'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l7 (p) l4
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L39 (P) L48'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L41 (P) L52'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L42 (P) L54'
L8 0 L7 (P) L4

=> s (metabolic disorder) or diabetes or (impaired glucose tolerance) or (diabetic neuropathy) or
L9 790513 (METABOLIC DISORDER) OR DIABETES OR (IMPAIRED GLUCOSE TOLERANCE) OR (DIABETIC NEUROPATHY) OR NEPHROPATHY

=> d his

(FILE 'HOME' ENTERED AT 19:59:44 ON 16 JAN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 20:00:10 ON 16 JAN 2003
L1 5816 S (DIPEPTIDYL PEPTIDASE IV) OR (DP IV)
L2 1726 S L1 (P) INHIBIT?
L3 14 S L2 (P) (UNSTABLE OR MASKED)
L4 5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)
L5 0 S (DIPEPTIDYL ALKYL KETONE)
L6 1 S (DIPEPTIDYL FLUOROALKYL KETONE)OR (DIPEPTIDYL CHLOROALKYL KE
L7 2933765 S ACETATE OR SUCCINATE OR TARTRATE OR FUMARATE OR PHOSPHATE OR
L8 0 S L7 (P) L4
L9 790513 S (METABOLIC DISORDER) OR DIABETES OR (IMPAIRED GLUCOSE TOLERAN

=> s l4 (p) l9
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L68 (P) L59'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L72 (P) L61'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L74 (P) L62'
L10 1 L4 (P) L9

=> d l10 1 ibib abs

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:819402 CAPLUS
DOCUMENT NUMBER: 132:36038
TITLE: Synthesis of prodrugs of ***unstable*** ***dipeptidyl*** ***peptidase*** ***IV*** ***inhibitors*** for use in treating ***diabetes***
INVENTOR(S): Demuth, Hans-Ulrich; Schmidt, Jorn; Hoffmann, Torsten; Glund, Konrad
PATENT ASSIGNEE(S): Probiodrug Gesellschaft Fur Arzneimittelforschung m.b.H., Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967279	A1	19991229	WO 1999-EP4381	19990624
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19828114	A1	20000127	DE 1998-19828114	19980624
CA 2335978	AA	19991229	CA 1999-2335978	19990624
AU 9947772	A1	20000110	AU 1999-47772	19990624
BR 9911415	A	20010320	BR 1999-11415	19990624
EP 1090030	A1	20010411	EP 1999-931163	19990624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002518518	T2	20020625	JP 2000-555930	19990624
NO 2000006483	A	20001219	NO 2000-6483	20001219
US 2001020006	A1	20010906	US 2000-745883	20001221

PRIORITY APPLN. INFO.: DE 1998-19828114 A 19980624
WO 1999-EP4381 W 19990624
OTHER SOURCE(S): MARPAT 132:36038
GI

/ Structure 3 in file .gra /

AB The invention relates to compds. of ***unstable*** ***inhibitors*** of ***dipeptidyl*** ***peptidase*** ***IV*** (***DP*** ***IV***) which comprise general formula A-B-C, whereby A represents an amino acid, B represents the chem. bond between A and C or an amino acid, and C represents an ***unstable*** ***inhibitor*** of ***DP*** ***IV*** . Such compds. are used for treating altered glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, ***diabetes*** mellitus, ***diabetic*** ***neuropathy*** , ***nephropathy*** , and secondary diseases in mammals caused by ***diabetes*** mellitus. Thus, (I) was reacted with pyridine to give [(II); R = Cbz], which was deprotected to give II (R = H)(III) which is thought to undergo an intramol. cyclization (no data) to form the active ***DP*** ***IV*** ***inhibitor*** . In 0.1 M HEPES-buffer, pH 7.6, at 25.degree., III had a half life (before self-cyclization) of 13.3 min.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 19:59:44 ON 16 JAN 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 20:00:10 ON 16 JAN 2003

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L1          5816 S (DIPEPTIDYL PEPTIDASE IV) OR (DP IV)
L2          1726 S L1 (P) INHIBIT?
L3            14 S L2 (P) (UNSTABLE OR MASKED)
L4             5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)
L5             0 S (DIPEPTIDYL ALKYL KETONE)
L6             1 S (DIPEPTIDYL FLUOROALKYL KETONE)OR  (DIPEPTIDYL CHLOROALKYL KE
L7       2933765 S ACETATE OR SUCCINATE OR TARTRATE OR FUMARATE OR PHOSPHATE OR
L8             0 S L7 (P) L4
L9        790513 S (METABOLIC DISORDER) OR DIABETES OR (IMPAIRED GLUCOSE TOLERAN
L10            1 S L4 (P) L9

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                                95.04      95.25

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                                -2.60      -2.60

STN INTERNATIONAL LOGOFF AT 20:13:05 ON 16 JAN 2003
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